middle - pioglitazone - treated group (Group P, n=10). Atherosclerosis was induced in all rabbits by intermittent high-cholesterol diet and endothelial denudation. From the ninth week, the rabbits in group P received pioglitazone (10 $mg \cdot kg^{-1} \cdot d^{-1}$) in addition to the diet, till the end of experiment. PET/CT scans were performed at 8 week and 18 week in all survival rabbits, to obtain FDG uptake parameters (mean standardized uptake value, SUVmean and maximal standardized uptake value, SUVmax). Concomitantly, serum samples were obtained for analysis of blood glucose (G), triglycerides (TG), total cholesterol (Ch), HDL, LDL, hs-CRP and MMP-9. All survival rabbits underwent 2 pharmacological triggerings to induce plaque rupture at 18 week. After pharmacological triggering, all rabbits were euthanatized, aortic histopathological analysis were performed.

CONCLUSIONS Pioglitazone can decrease the incidence of thrombotic events and attenuate plaque vulnerability by ways of modulating vascular inflammation, decreasing plaque area and neovessels. 18F FDG PET/CT, seems capable of monitoring inflammation in asses anti-atherosclerotic effect of pioglitazone.

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GW26-e0186

Triptolide inhibits angiotensin II induced cardiac fibroblasts proliferation by down-regulating TGF-β1/Smad3 pathway

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OBJECTIVES Previous studies have indicated that immune-inflammatory activation plays an important role in the development of myocardial remodeling in patients with chronic heart failure. Cardiac fibroblast (CFb) plays a central role in the pathogenesis of myocardial fibrosis. Triptolide (TPL), PG-490, is a diterpene triepoxide with potent immunosuppressive and anti-inflammatory properties and has been used in China for centuries to treat immune-related disorders. However, the effects of TPL on myocardial fibrosis remain unclear. The objective of this study was to determine whether TPL can protect myocardial fibrosis by inhibiting the proliferation of CFbs.

METHODS Myocardial tissue in newborn rats was digested with low concentration trypsin and collagenase. The CFbs and myocardial cells were isolated with differential adherence method. Angiotensin II (10^{-7} mol/L) was used to promote the proliferation of CFbs. TPL (100 ng/ml) was applied for 48 hours to inhibit CFbs proliferation. MTT assay was used to detect cell survival rate *in vitro*. Flow cytometry was performed to analyze apoptosis. Collagen concentration was measured using the hydroxyproline assay kit. Quantitative real-time PCR was used to detect the expression of TGF-β1 and Smad3.

RESULTS Compared to the control group, CFbs in the angiotensin II treated group proliferated significantly. However, compared to the angiotensin II treated group, the cell survival rate (324.64±157.95% *vs.*123.38±34.32%, P<0.01) and collagen concentration (10.67±4.03 μg/ml *vs.* 4.40±1.49 μg/ml, P=0.01) in TPL treated group were significantly lower. TPL treatment also promoted apoptosis in angiotensin II treated CFbs. The apoptosis rates of the angiotensin II and TPL treated groups were 0.92±0.61% and 4.32±0.43%, respectively. Furthermore, compared against the angiotensin II treated group, TPL treatment down-regulated the expression of TGF-β1 (1.36±1.22 *vs.* 0.66±0.15, P<0.01) and Smad3 (1.53±0.14 *vs.* 0.25±0.10, P<0.05) mRNA levels significantly in rat CFbs *in vitro*.

CONCLUSIONS Our findings indicate that TPL may inhibit angiotensin II induced cardiac fibroblast proliferation by down-regulating the TGF-β1/Smad3 signaling pathway. TPL may be a potential therapeutic drug for myocardial fibrosis.

GW26-e0254

Effect of early treatment with L-carnitine on left ventricular function and hemodynamics after acute myocardial infarction in SD rats

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OBJECTIVES L-carnitine is a carrier in the course of the fatty acids Metabolism. The fatty acids Metabolic Processes is damaged when myocardial ischemia. The aim of this study is to determine the effects of L-carnitine with different dosage on left ventricular function and hemodynamics in AMI rats.

METHODS AMI were conducted by ligating left anterior descending branch in male SD rats. Rats were randomly assigned to one of the following groups: AMI control group(n=12), large dosage L-carnitine group (120mg•100g-1•d-1, n=12), middle dosage L-carnitine group (60mg•100g-1•d-1, n=13), small dosage L-carnitine group(30mg•100g-1•d-1, n=11). Sham operated rats(n=10) were selected randomly as non-infarction control group. L-carnitine was administered by direct abdominal cavity's injection for four weeks. Then echocardiography examination and hemodynamic studies were performed.

RESULTS

1. Compared with the AMI groups, a significant increase could be seen in ejection fraction(EF, 68.08±5.98%, 68.20±5.52% ,65.35±12.07% respectively) and fractional shortening (FS, 33.47±4.24%, 34.52±4.19%, 31.38±7.60% respectively) among in small, middle and large dosage L-carnitine groups(all P<0.01), and a significant decrease could be seen in left ventricular end-diastolic volume(LVEDV, 0.58±0.13ml, 0.63±0.27ml, 0.65±0.20ml respectively) and left ventricular end- systolic volume(LVESV, 0.17±0.08ml, 0.20±0.12ml, 0.21±0.11ml respectively) in small, middle and large dosage L-carnitine groups, no significant difference among the three L-carnitine groups(P>0.05).
2. Compared with the AMI group, a significant decrease could be seen in left ventricular end-diastolic pressure (LVEDP, 0.92±9.06mmHg, 2.72±4.32mmHg, 2.99±7.45mmHg respectively)(all P<0.01), and a significant increase could be seen in left ventricular pressure maximal rate of rise (+dp/dt, 4646.02±650.26mmHg/s, 4821.39±956.18mmHg/s, 4544.87±617.77mmHg/s respectively) (P<0.05), left ventricular pressure maximal rate of fall(-dp/dtmax, 4358.25±700.65mmHg/s, 4360.79±754.10mmHg/s, 4409.26±929.50mmHg/s respectively), and left ventricular systolic pressure(LVSP, 84.85±6.22mmHg, 85.17±7.22mmHg, 87.42±12.31 mmHg respectively), no significant difference in these indexes among the small, middle and large dosage L-carnitine groups, and no significant difference in aortic systolic blood pressure(ASBP), aortic diastolic blood pressure(ADBP), mean aortic pressure(MAP) and heart rate (HR) among the three L-carnitine groups.

CONCLUSIONS Early treatment with L-carnitine in three dosages could improve hemodynamic state and left ventricular function effectively in AMI rats.

GW26-e1235

Study on the method of isolation and culture of rat cardiac stem cells in vitro

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OBJECTIVES To find the best method of cardiac stem cell (CSC) isolation and culture through comparing the effect of different methods in laying cell adhesion agent and different serum concentrations in culture.

METHODS Experiment was conducted with healthy newborn wistar rats (one day of birth). The heart tissues were digested with trypsin and collagenase repeatedly after it was removed from the rat chest under sterile conditions, then the digested tissues were cultured in cell culture bottle laying with fibronectin (FN). The first passage cells were cultured in the bottle laying with Poly -D- lysine (PDL). Compare of the CSC numbers and proliferation was conducted among different cell groups, which were the group cultured in bottles laying at 37 °C with the other one laying at room temperature, and the group cultured by modified cardiosphere growing medium (CGM)(prescription is IMDM, 11% fetal bovine serum, 1% penicillin and streptomycin, 1% L- glutamic acid) with the other one by normal CGM (prescription is IMDM, 10% fetal bovine serum, 1% penicillin and streptomycin, 1% L- glutamic acid). The CSCs were identified by immunohistochemistry.

RESULTS CSCs were isolated from myocardial tissue of neonatal rats successfully, C-kit positive. FN and PDL coating at 37°C can significantly promote cell adhesion, increase cell growth rate and reduce the cell doubling time (p<0.05) comparing with that at room temperature. Application of modified CGM may accelerate cell growth speed and reduce the cell doubling time (p<0.05).

CONCLUSIONS Isolation and culture of primary CSCs with 37°C coating cell culture bottles and modified CGM is a more superior method, which lays the foundation for the further experimental study.

GW26-e1432

Effect of Rosiglitazone on Insulin Resistance and ROS/IKK Signaling Pathway in Vascular Endothelial Cells

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OBJECTIVES To explore the protective effect of rosiglitazone on insulin resistance (IR) induced by high glucose in vascular endothelial cells and its possible mechanism.

METHODS Human umbilical vein endothelial cells (HUVECs) was divided into 3 groups: the normal control group cultivated in DEME medium with 5.5 mmol/L glucose; the high glucose group (HG) cultivated in DEME medium with 33 mmol/L glucose for 24 h after the IR model was set up; the rosiglitazone group cultivated in DEME medium with 33 mmol/L glucose and 10 μmol/L of rosiglitazone for 24 h after the IR model was set up. The cell viability, nitric oxide(NO), endothelin-1(ET-1), mitochondrial membrane potential, reactive oxygen species(ROS), p-IKK and IkBa protein levels were detected.

RESULTS Compared with the normal control, the cell viability, the level of NO and the mitochondrial membrane potential were decreased, levels of ET-1 and ROS increased, p-IKK expression was upregulated, and IκBα expression was down-regulated in HG group(all $P<0.01$). Rosiglitazone reversed these changes($P<0.05$).

CONCLUSIONS Rosiglitazone has the protective effect on insulin resistance induced by high glucose in vascular endothelial cells via inhibiting ROS/IKK signaling pathway.

GW26-e2914

A study of the mechanism of valsartan pre-protecting adriamycin-induced cardiotoxicity

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OBJECTIVES To investigate the effects of valsartan pre-protects adrimycin-induced cardiotoxicity and the mechanism.

METHODS 61 of 8w SD rats were devided into 4groups as follows: Control group (n=9) were feeded normally; adrimycin-induced cardiotoxicity() group:intraperitoneal ADR,2.5mg/(kg.w), totally 6 weeks, cumulative dose was 15mg/kg. Group C (n=17): valsartan (low dose) intervened (VLD) group, Group D: valsartan(high dose) intervened group(VHD). In group C and D, valsartan was separately (10mg/(kg.d) and30mg/(kg.d)) given from the first dose of adriamycin, totally 6 weeks. After 6 weeks administration of valsartan and adriamycin, observed 4 weeks. Use echocardiography to detect LVEF, LVFS, LVESD, LVEDD. Take the heart out of the chest to do measure hearts' weight. And then do HE, Sirius red staining. Count out CVF. Use ELISA kits to detect the content of RAS and ROS in cardiac tissues. Use qRT-PCR to detect collagen I, collagen III, caspase3 and caspase8's expressions.

RESULTS

(1) Compared with blank control group, renin, angiotensin II, aldosterone synthase, ROS in the myocardial tissues of the model group are evidently overexpressed ($P<0.05$); In group model, rats' myocardial tissue, caspase3, caspase8 mRNA levels increased significantly ($P<0.05$), the myocardial collagen volume increased significantly ($P<0.05$).
(2) Valsartan high dose group compared with blank control group, there was no significant statistical differences about indexes above ($P>0.05$). compared with model control group, the valsartan high dose group and the blank control group, there were significant differences about the above indexes ($P < 0.05$).
(3) There were no significant differences in LVEDD among the four groups ($P>0.05$); About LVESD, LVEF, LVFS, there were no significant difference between the valsatan low dose group and the model control group. The above index average were less than the model control group and the valsartan low dose group, The differences among the three groups were significant ($P<0.05$), Compared with the high dose group and the blank control group, the above indexes in model control group were higher. The differences were significant($P<0.05$). There were no difference between the valsartan high dose group and blank control group ($P>0.05$).

CONCLUSIONS

(1) Adriamycin might via activing RAS in rats' myocardial tissues to cause angiotensin overexpressed. Angiotensin-stimulatied to generate more ROS. So the superabundant ROS caused the myocardial apoptosis and fibrosis.
(2) Appling enough dose (load dose) valsartan from the first dose of adriamycin could against AT1 in rats' myocardial tissues. So it could down-regulate the expression of NOX1 and NOX4 and the ROS decreased. In the end, the myocardial apoptosis and fibrosis would be alleviated. However early application of small dose valsartan had no protective effect on adriamycin induced cardiotoxicity.
(3) Sufficient and early use of valsartan in adriamycin chemotherapy rats could prevent rats suffering Cardiotoxicity. The mechanism might related to NOX1 and NOX4 mediated oxidative stress.

GW26-e2924

Endothelial progenitor cells join in HHcy impaired angiogenesis

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OBJECTIVES During the last decade, we and others have demonstrated that HHcy can inhibit endothelial cell growth and postinjury reendothelialization, accelerate neointimal formation, also can impair endothelial relaxation, stimulate vascular smooth muscle cell proliferation, and inhibit high-density lipoprotein biosynthesis. However, the fundamental basis of HHcy-impaired angiogenesis remains unknown, especially the role of endothelial progenitor cells in angiogenesis.

Role of endothelial progenitor cell in HHcy impaired angiogenesis. Intravenous transfusions of Sca-1+ cells maybe play a role in HHcy MI mice angiogenesis.

METHODS

1. Angiogenesis of HHcy mice under myocardial infarction. 1.1 Cardiac function was measured with echocardiography (VisualSonics Vevo 770); 1.2 Hearts were moved at 2 weeks/6 weeks after myocardial infarction and kept at -80°C until needed. Frozen heart tissues were cut into 5μm thick slices. Adjacent sections (taken at the midpoint between LAD ligation site and apex) were stained with rabbit polyclonal antibodies against CD31.

2. Flow cytometry analysis. A volume of 200μl peripheral blood/bone marrow were incubated for 30 minutes in the dark with monoclonal antibodies against mouse vascular endothelial growth factor receptor 2 (VEGFR2) followed by PE-conjugated secondary antibody.

3. MACS Separation-purify Sca-1+ cells. Purity of Sca-1+ cell is based on the use of MACS MicroBeads, MACS Columns and MACS Separators.

4. Intravenous transfusions of Sca-1+ cells in HHcy MI mice angiogenesis. To evaluate the homing to infarcted heart of injected cells, 200μl purified Sca-1+ cells were labeled with CellVueR NIR (near-infrared) 780 (Excitation max: 745nm/Emission max: 776nm, Mol. Targeting Tech. Inc. West Chester, PA) and injected peri-orbitally into C57/B6 mice, 6 hours before MI procedure.

RESULTS

1. HHcy impairs mouse cardiac function. Ejection fraction (EF) and fractional shortening (FS) were lower in HHcy mice group than control group, as well as heart capillary density. HHcy mice hearts have depressed function and less capillary density after myocardial infarction stress. Survival rate is also lower in HHcy mice.

2. Peripheral blood derived EPC percentage decreased in HHcy mice group and bone marrow derived EPC percentage is higher in HHcy mice group, but cell death rate is also higher in HHcy mice.

3. Intravenous transfusion of Sca-1+ cells treatment induce PB derived EPC percentage increase in both control mice group and HHcy mice group. 6 weeks survival rate increased from 12.5% to 27.3% in hCBS+Cbs-/- cell treat group, and also 62.5% to 80% in hCBS+Cbs+/- cell treat group; The LVEF increased from 19.3% to 38.5% in hCBS+Cbs-/- cell treat group, and also 31.6% to50.9% in hCBS+Cbs+/- cell treat group.

CONCLUSIONS EPC joined angiogenesis after myocardial infarction which is so important to cardiac function. Cell treatment restores ischemia-induced angiogenesis in HHcy mice.

GW26-e3551

Plaque Thrombosis Are Reduced by Attenuating Plaque Inflammation with Pioglitazone and Are Evaluated by Fluorodeoxyglucose Positron Emission Tomography

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